

REMARKS

Claims 1-24 are in the application. Of these, Claims 1-11 were in the application, and Claims 12-24 have been added to make the claims single-dependent, as opposed to multiple-dependent. In all, Applicants have amended the application to adapt it to format of U.S. applications. More specifically, Applicants have amended the specification to provide a brief description of the drawings, and have further amended the claims to adapt them to the format of U.S. applications.

Discussed hereunder is how the amended claims avoid or overcome the prior art including the references cited by the Examiner to support the art rejection. Claims 1-4 stand rejected under 35 USC 103(a) as being unpatentable over [Himmler, reference N] Bartel, (US 6,278,013).

The rejection is based on the finding that "[T]he difference between the prior art compound and the instantly claimed compounds is the extent of salt formation...." The conclusion of unpatentability is based on the grounds that: "It's axiomatic in organic chemistry that acids will react with bases to form salts. Since there are several nitrogen atoms present in the instant compound, it is possible to form 1 to 3 acid-addition salts of HCL."

Applicants traverse the rejection because the possibility of forming 1 to 3 acid-addition salts does not render obvious the claim-recited semihydrochlorides. In this regard, Applicants direct the Examiner's attention to the distinction over the art-related compounds, as found in their specification at page 2, line 10 through page 4, line 19. Notably, the specification states that CCDC of formula (I), which is the referenced compound, can be used to prepare solutions in water of about 0.02% strength (w/w). The specification further states that CCDC hydrochlorides of formula IV, having different X-ray powder diffractogram, a different IR spectrum and a different melting point range (determined by differential thermoanalysis) are known in the art.

Distinctly, at page 4, line 20, the specification avers that the claim-recited CCDC semihydrochlorides of formula (VI) have a different X-ray powder diffractogram, a different IR spectrum and a different melting point range (determined by differential thermoanalysis) and notably a markedly high solubility in

water. More specifically, the referenced compound can be used to prepare solutions in water having a strength of 0.19% (w/w). This is a surprising improvement over the solubility 0.02% (w/w) for the referenced compound.

Thus, the issue here is whether there is a basis in Bartel for the skilled artisan to modify starting compounds or the salts thereof to the claim-recited semihydrochlorides with a reasonable expectation of success.

It is well established that prima facie obviousness has to be supported by evidence or practical reason of record which would have led the skilled artisan to the claims with a reasonable expectation of success.

Other than the statement that acids would react with bases to form salts, the Examiner has not pointed to reasons for modifying the prior art product to CCDC semihydrochlorides. The mere fact that the structure in the primary prior art reference could have been modified to form the claimed structure would not have made the modification obvious unless the prior art suggests the desirability of the modification, In re Laskowski 10 USPQ 2d 1397 (Fed. Cir. 1989). In this case there is no basis for the belief that one might arrive at the semihydrochlorides by selecting specific items and conditions leading thereto, Ex Parte Kuhn (POBA 1961) 132 USPQ 359. Therefore, the claims are not rendered obvious by the cited reference.

At any rate, as noted above the surprising improvement in solubility to 19% over the prior art 0.02% rebuts any presumption of obviousness.

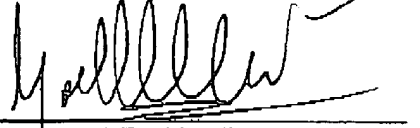
In view of the foregoing amendments and remarks, Applicants submit the claims are patentably distinct and therefore pray for their allowance.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is titled "VERSION WITH MARKINGS TO SHOW CHANGES MADE".

Applicants request the examination and allowance of the claims.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE**IN THE SPECIFICATION:**

At page 6, line 5 of the specification insert the following:

-BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the X-ray powder diffractogram of CCDC hydrochloride of the formula (IV) .

Figure 2 shows the differential thermodiagram of the melting point, determined by DTA, of CCDC hydrochloride of the formula (IV) being from 305°C to 307°C (with decomposition).

Figure 3 shows the IR spectrum measured in KBr of CCDC hydrochloride of formula (IV).

Figure 4 shows the X-ray powder diffractogram of CCDC semihydrochloride of the formula (VI).

Figure 5 shows the differential thermodiagram of CCDC semihydrochloride of formula (VI) obtained by the procedure of Example 1, having a melting point of 278 to 280°C determined by differential thermoanalysis.

Figure 6 shows the IR spectrum, measured in KBr of the CCDC semihydrochloride of the formula (VI).--

IN THE CLAIMS:

Claims 2 - 11 have been amended as follows:

2. Semi-hydrochloride of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo-[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid (CCDC semihydrochloride), having ~~characterized in that it has~~ an X-ray powder diffractogram with the following reflection signals (2 theta) of high and medium intensity.
3. Semi-hydrochloride of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo-[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid (CCDC semihydrochloride), having ~~characterized in that it has~~ an X-ray

powder diffractogram with the following reflection signals (2 theta) of high and medium intensity.

2 θ (2 Theta)

5.86
6.90
7.26
8.98
9.35
10.13
10.68
10.97
12.41
13.67
14.57
14.89
15.73
16.07
16.47
16.87
17.78
18.91
19.81
20.04
20.62
20.75
20.93
21.46
21.74
22.92
25.36

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25.71

26.98

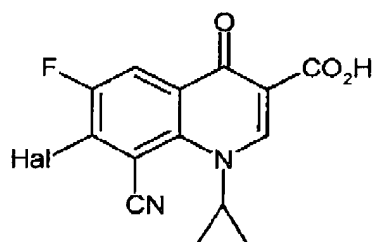
27.58

28.24

30.61

and a melting point, determined by DTA, of from 278°C to 280°C.

4. CCDC semihydrochloride according to Claim 1 or 2, obtainable by reacting 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinoline-carboxylic acid of the formula (II)

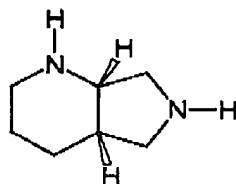


(II),

in which

Hal represents fluorine or chlorine,

and (1S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)

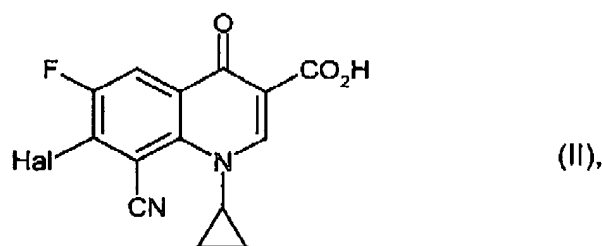


(III),

optionally if appropriate in the presence of a base, in one of the following diluents or diluent mixtures:

- a) aliphatic alcohols having at least four carbon atoms,
 - b) mixture of, ~~for example~~, aliphatic alcohols having at least three carbon atoms with the diluent N-methylpyrrolidone,
 - c) mixture of propanol and N,N-dimethylformamide,
- or
- d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

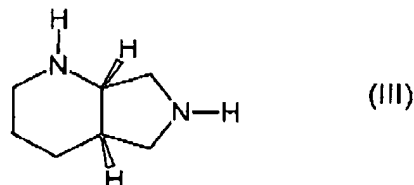
5. Process for preparing CCDC semihydrochloride according to Claim 1 comprising reacting any of ~~Claims 1 to 4, characterized in that~~ 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (II)



in which

Hal represents fluorine or represents chlorine

and (1S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



are reacted in the presence of a base in one of the following diluents or diluent mixtures:

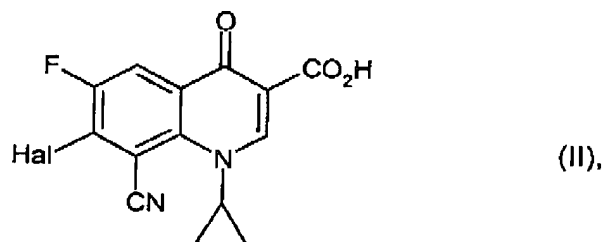
- a) aliphatic alcohols having at least four carbon atoms,
 - b) mixture of, ~~for example,~~ aliphatic alcohols having at least three carbon atoms with the diluent N-methylpyrrolidone,
 - c) mixture of propanol and N,N-dimethylformamide,
- or
- d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

- 6. Process for preparing CCDC semihydrochloride according to Claim 5, wherein ~~characterized in that~~ the diluent used is an aliphatic alcohol having at least 4 carbon atoms or that an aliphatic alcohol having at least two carbon atoms is used as component of a diluent mixture.
- 7. Process for preparing CCDC semihydrochloride according to Claim 5, wherein ~~characterized in that~~, if an aliphatic alcohol having at least 3 carbon atoms is used as component of a diluent mixture, N-methyl-pyrrolidone is simultaneously employed as a further diluent in a ratio of from 1 to 1 to 3 to 1.

8. Process for preparing CCDC semihydrochloride according to Claim 6, wherein characterized in that, if propanol is used as component of a diluent mixture, N,N-dimethylformamide is simultaneously employed as further diluent in a ratio of from 1 to 1 to 3 to 1.
9. Medicament, characterized in that it comprises, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 1 ~~any of Claims 1 to 4~~.
10. A method of preparing a medicament comprising formulating Use of CCDC semihydrochloride according to Claim 1 ~~any of Claims 1 to 4 for preparing medicaments~~.
11. A process for treating bacteria comprising applying thereto an antibacterial composition containing Use of CCDC semihydrochloride according to Claim 1 ~~any of Claims 1 to 4 in antibacterial compositions~~.

The following new claims have been added:

- 12. CCDC semihydrochloride according to Claim 2, obtainable by reacting 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinoline-carboxylic acid of the formula (II)

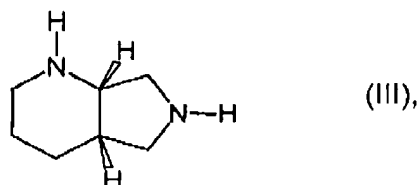


in which

Hal represents fluorine or chlorine,

Hal represents fluorine or chlorine,

and (1S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



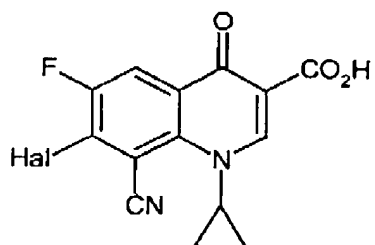
optionally in the presence of a base, in a one of the following diluents or diluent mixtures:

- a) aliphatic alcohols having at least four carbon atoms,
- b) mixture of aliphatic alcohols having at least three carbon atoms with N-methylpyrrolidone,
- c) mixture of propanol and N,N-dimethylformamide,

or

- d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

13. Process for preparing CCDC semihydrochloride according to Claim 2, characterized in that 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (II)

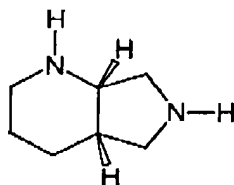


(II),

in which

Hal represents fluorine or represents chlorine

and (1S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



(III)

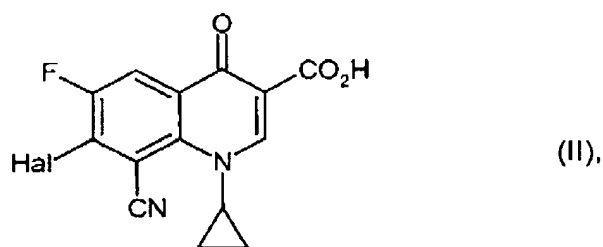
are reacted in the presence of a base in one of the following diluents or diluent mixtures:

- a) aliphatic alcohols having at least four carbon atoms,
- b) mixture of aliphatic alcohols having at least three carbon atoms with N-methylpyrrolidone,
- c) mixture of propanol and N,N-dimethylformamide,

or

- d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

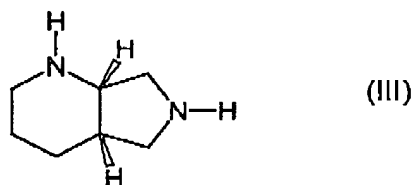
14. Process for preparing CCDC semihydrochloride according to Claim 3, characterized in that 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (II)



in which

Hal represents fluorine or represents chlorine

and (1S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)

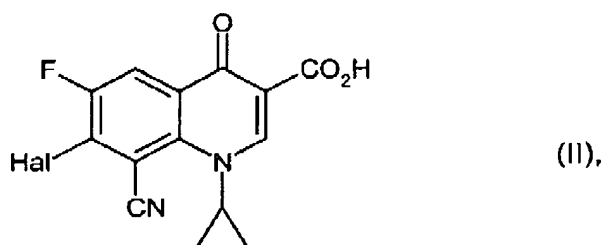


are reacted in the presence of a base in one of the following diluents or diluent mixtures:

- a) aliphatic alcohols having at least four carbon atoms,

- b) mixture of aliphatic alcohols having at least three carbon atoms with N-methylpyrrolidone,
- c) mixture of propanol and N,N-dimethylformamide,
- or
- d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

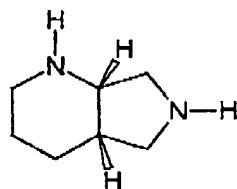
15. Process for preparing CCDC semihydrochloride according to Claim 4, characterized in that 7-halogeno-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (II)



in which

Hal represents fluorine or represents chlorine

and (1S,6S)-2,8-diazabicyclo[4.3.0]nonane of the formula (III)



(III)

are reacted in the presence of a base in one of the following diluents or diluent mixtures:

- a) aliphatic alcohols having at least four carbon atoms,
 - b) mixture of aliphatic alcohols having at least three carbon atoms with N-methylpyrrolidone,
 - c) mixture of propanol and N,N-dimethylformamide,
- or
- d) mixture of ethanol with N-methyl-pyrrolidone with added tripropylamine, tributylamine, N-ethylmorpholine, N-propylmorpholine and/or N-butylmorpholine base.

- 16. Medicament, characterized in that it comprises, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 2.
- 17. Medicament, characterized in that it comprises, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 3.
- 18. Medicament, characterized in that it comprises, in addition to customary auxiliaries and excipients, CCDC semihydrochloride according to Claim 4.

19. A method of preparing a medicament comprising formulating CCDC semihydrochloride according to Claim 2.
20. A method of preparing a medicament comprising formulating CCDC semihydrochloride according to Claim 2.
21. A method of preparing a medicament comprising formulating CCDC semihydrochloride according to Claim 1.
22. A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride according to Claim 2.
23. A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride according to Claim 3.
24. A process for treating bacteria comprising applying thereto an antibacterial composition containing CCDC semihydrochloride according to Claim 4.--